

REMARKS/ARGUMENTS:

Claims 1-54 are pending in the application. Claims 1-31, 33, 37 and 46-54 are withdrawn from consideration. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Claim Rejection Under 35 U.S.C. § 102:

Claims 32-36 and 38-45 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Bennett et al. (U.S. Patent No. 6,066,500). The Applicant respectfully traverses this rejection.

Claim 32 is as follows:

A method for inhibiting the expression of a target gene in a substrate that expresses the targeted gene, comprising the steps of:

- a) providing a composition comprising an mRNA-cDNA hybrid capable of inhibiting the expression of said targeted gene in said substrate; and
- b) contacting said substrate with said composition under conditions such that the expression of said gene in said substrate is inhibited.

Applicant respectfully submits that Bennett cannot anticipate claim 32, because Bennett fails to teach providing a composition comprising an mRNA-cDNA hybrid capable of inhibiting the expression of a target gene in a substrate. In Bennett, the antisense oligonucleotides are single stranded, whereas the mRNA-cDNA hybrid of the present invention is double stranded. The antisense compounds of Bennett

“preferably comprise from about 8 to about 30 nucleobases (i.e. from about 8 to about 30 linked nucleosides). Particularly preferred antisense compounds are antisense oligonucleotides, even more preferably those comprising from about 12 to about 25 nucleobases.” (Bennett, column 5, line 65-column 6, line 3).

Bennett cannot make instant claim 32 obvious. Bennett has no teaching or suggestion whatsoever of providing a composition comprising an mRNA-cDNA hybrid, much less of using this oligonucleotide duplex for inhibiting the expression of a targeted gene. In Bennett, any hybridization takes place after the antisense compound is administered. (Bennett, column 3, lines 7-36; column 5, lines 16-28).

It is the discovery of the present invention that the mRNA-cDNA hybrids of the present invention are capable of silencing specific gene expression through an intracellular defense mechanism termed posttranscriptional gene silencing (PTGS) or RNAi. It is proposed that the mRNA-cDNA hybrids effect an RdRp-dependent gene silencing phenomenon, i.e., DNA-RNA interference (D-RNAi). The advantages of using D-RNAi instead of ds-RNA are as follows: 1) the cDNA part of a D-RNAi can be modified by nucleotide-analog incorporation to increase the stability and effectiveness of transfected probe activities; 2) the RdRp enzyme may provide higher affinity to the mRNA template of a D-RNAi compared to a ds-RNA due to lower binding interaction between DNA-RNA duplexes than RNA-RNA duplexes; and 3) the cDNA part of a D-RNAi provides further antisense gene knockout activity in addition to the PTGS gene silencing mechanisms of the sense-RNA template, resulting in multiple specific gene interference effects with one probe. (Applicant's

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specification, at page 12, lines 16-26). The process of posttranscriptional gene silencing (PTGS) or RNAi of the present invention is different from the direct hybridization of an antisense oligonucleotide to its target mRNA, which is taught by Bennett.

In light of the foregoing, Applicant respectfully submits that Bennett could not have anticipated or rendered obvious claim 32, because Bennett fails to teach or suggest each and every claim limitation. Claims 33-36 and 38-45 depend from claim 32 and cannot be anticipated or rendered obvious for at least the same reasons as claim 32. Withdrawal of this rejection is thus respectfully requested.

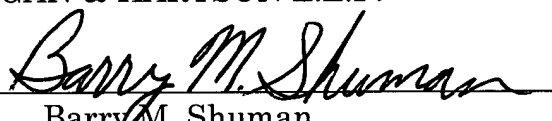
In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

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By: 
Barry M. Shuman
Registration No. 50,220
Attorney for Applicant(s)

500 South Grand Avenue, Suite 1900
Los Angeles, California 90071
Telephone: 213-337-6700
Fax: 213-337-6701